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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/932,834	09/18/97	PORUBER D	077319/0129

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EXAMINER	
BERCH, M	

ART UNIT	PAPER NUMBER
1611	27

DATE MAILED: 11/27/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/932,834	Applicant(s) Porubek
	Examiner Mark L. Berch	Group Art Unit 1611

☒ Responsive to communication(s) filed on *10/26/98* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-7 and 9-27* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7 and 9-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Applicants are reminded of the proper format for amending claims, All subject matter added to a claim must be underscored. The new species added to the beginning of claim 1 was not.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9-27 are rejected under 35 U.S.C. 112, paragraphs 1 and 2, as the claimed invention is not described, or is not described in such full, clear, and exact terms as to enable any person skilled in the art to make and use the same, and/or failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. Specifically:

1. Formula II has been incorrectly copied in Claim 1. The subscript n is in the wrong place and the leading bond is missing.

2. Replacement of "carboxy" with "carboxylic acid moiety" simply reinstates the original problem. This is presumably derived by the removal of a hydrogen from a

carboxylic acid, but from which carboxylic acid? And what kind of H? Could it be a H from NH or SH? Could it be the acidic H from the carboxy function?

3.There still remains previous point 10; the traverse on this point is unpersuasive. Applicants point to pages 5-9, but these provide no explanation at all. The term appears once at page 6, line 17, but no explanation is set forth.

4. The third Claim 14 structure was miscopied; the extreme left should have a methoxy group.

5. There still remains previous point 19; the traverse on this point is unpersuasive. Applicants point to Q as substituted alkenyl, but that is mistaken. R_4 in this species corresponds to O<u>CH</u>H(Phenylvinyl). The underscored carbon corresponds to the X = C choice. The underscored Hydrogen means that R_4 <u>must</u> be the OXR_5H choice, since only that OXR_5H choice will provide for the underscored H --- remember, it was added to provide for the H. However, in the OXR_5H choice, the X, that is, the C, has only three things attached: O, H, and R_5. Since Carbon is tetravalent, R_5 must be divalent, to provide for bonds three and four, and the only divalent choice is oxo. To put it another way, the OXR_5H choice when X is C corresponds ONLY to the formyloxy group.

6. The term "mercaptoalkoxy" has appeared in Claim 6, last line, without description. The term does not appear in the specification. If another term is being relied on, applicants must show that one of ordinary skill in the art would have been sure that this is what was truly intended.

Claims 1-7, 9-27 are rejected 35 USC 112, paragraph 1 for lack of enablement, in terms of how to use. The reasons were given previously; the traverse on this point is unpersuasive.

Applicants make three numbered points at the top of page 15:

1. Compound claims "embody non-therapeutic utilities." Where does the specification teach such utilities?

2. "Enablement must be evaluated taking into account claims scope." Agreed, but this works out to an argument against enablement. The claims are so broad that it is impossible to accurately even estimate their scope. R_2 and R_3, taking into account their replacement-by-oxygen and branching possibilities easily have a thousand choices each. Just <u>one</u> of the possibilities for R_4 is $OX(R_5)_m$. R_5 is Q which has an immense range. Just <u>some</u> of the choices are optionally substituted alkyl, alkenyl, alkynyl, alkoxy, oxoalkyl, carboxyalkyl, hydroxyalkyl, alkenyloxy, alkynyloxy, oxoalkyloxy, and certain heterocycles. There are easily a thousand such groups. The substitution is completely open-ended; one could easily imagine a thousand possible substituents. Thus, even limiting oneself to monosubstitution with the unnamed substituents, there are 10^6 Q choices, meaning that for just the possibility of X = C, m = 3, there are more than 10^{16} compounds; multiplied by the R_2 and R_3 choices, that comes to 10^{19}.

3. "Imputing therapeutic limitations for the purposes of evaluating enablement, or any other purpose, is improper." Its is not entirely clear what "imputing therapeutic

limitations" means. The examiner is not reading any limitations into the claims. Only a single utility will suffice for enablement.

Applicants state that "the Office improperly holds ... an enablement standard that can only be met with clinical data." This is simply not true. The examiner has not even mentioned clinical data.

Applicants state that "at least some embodied compounds are structurally similar to lisofylline, a drug which has been the subject of clinical investigation." This is true. But despite such investigation, which has really been quite extensive, no one has been able to figure out how to get lisofylline to actually work. That is clear evidence that getting these types of compounds to work requires undue experimentation. Even if this problem were finally to be solved tomorrow, that would not help, as the enablement must be established as of the filing date.

With regard to discussion of the dosage data in the specification, an impasse has clearly been reached.. Ranges of 10000 or 40000 fold are too large to be of value; again, see In re Gardner, 166 USPQ 138.

Applicants argue that any 1000 times a day administration is unreasonable. It is agreed, but that is what the low end of the dosage data works out to. Even at the high end, this comes to 25 administrations a day, which is also unreasonable. But this is based on what the specification says. The dosage data in the specification is internally inconsistent, because while the paragraph says 1-6 times a day, the actual

numbers given on size of doses and total administration work out to far more times than that.

Applicants refer to Examples 22-25, but with no explanation of how this will teach one of ordinary skill in the art how to get these compounds to work without undue experimentation. Thus, applicants state that "Example 25 provides treatment of dogs." Treatment of what? The dogs were not treated for anything. No determination was made of the effect of the drug upon the dog. This is no more than a pharmacokinetic study to determine what plasma levels of lisofylline were achieved. The examine agrees that the compounds tested are prodrugs for lisofylline, but as set forth above, getting lisofylline to actually work involves undue experimentation.

With regard to the prodrug issue, it is agreed that there is no "prodrug" limitation in the claims. The examiner's point, however, is that the specification presents these compounds as being prodrugs for lisofylline, even though many of the $X(R_5)_m$ and $X.(R_5)$ choices are obviously not going to cleave off. The entire thrust of pages 2-3 deals with trying to get a good prodrug for lisofylline; see e.g. page 3, lines 31-35, page 4, lines 8-9; page 5, lines 9-11.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718.

Mark L. Berch

Primary Examiner

Group 1610 - Art Unit 1611

November 25, 1998